REMARKS

It is respectfully requested that this application be reconsidered in view of the following remarks and that all of the claims remaining be allowed.

The Restriction Requirement:

In the Office Action, the Examiner required the following restriction under 35 U.S.C. § 121:

I. Claims 1-15 and 23-30, drawn to a method of detecting ras-activated neoplastic cells comprising determining whether a biological sample is permissive for reovirus infection, classified in class 435, subclass 5.

II. Claims 16-22 and 31-33, drawn to a method of treating a ras-activated neoplasm, classified in class 424, subclass 93.1.

In addition, if Group I is elected, the Examiner requires a further election of one of the following groups:

(i) Contacting the sample with serotype 3 Dearing strain reovirus.

(ii) Contacting the sample with avian reovirus.

(iii) Obtaining the sample from one of the cancers listed in claim 8.

(iv) Contacting the sample with reovirus.

(v) Contacting the sample with adenovirus having a VA1 mutation.

(vi) Contacting the sample with vaccinia having a K3L mutation.

(vii) Contacting the sample with vaccinia having a E3L mutation.

(viii) Contacting the sample with vaccinia having a K3L and a E3L mutation.

(ix) Contacting the sample with parapoxvirus orf viruses having a OV20.0L mutation.

(x) Contacting the sample with influenza virus having a NS-1 mutation.

(xi) Contacting the sample with herpes virus having a gamma 34.5 mutation.

(xii) Contacting the sample with vesicular stromatitis virus.

(xiii) Contacting the sample with ONYX-015 virus.

(xiv) Contacting the sample with Delta24 virus.

(xv) Any one of the neoplastic cell phenotypes listed in claim 26.

Alternatively, if Group II is elected, the Examiner requires a further election of one of the following groups:

(xvi) Avian reovirus.

(xvii) Adenovirus having a VA1 mutation.

(xviii) Vaccinia having a K3L mutation.

(xix) Vaccinia having a E3L mutation.

(xx) Vaccinia having a K3L and a E3L mutation.

(xxi) Parapoxvirus orf viruses having a OV20.0L mutation.

(xxii) Influenza virus having a NS-1 mutation; and herpes virus having a gamma 34.5 mutation.

(xxiii) Vesicular stromatitis virus.

(xxiv) ONYX-015 virus.

(xxv) Delta24 virus.

(xxvi) Any one of the neoplasms listed in claim 22.

(xxvii) Any one of the neoplasm phenotypes listed in claim 32.

The Election

In response to the restriction requirement, Applicants elect Group I, and further elect Group (iv), with traverse.

The restriction set forth in Group i-xxvii is respectfully traversed because (1) the Office Action does not list the claims in each group or classify the groups; (2) the reasons of "unrelated

inventions" provided by the Office Action are inconsistent with the claimed invention; and (3) there will not be a serious burden on the Examiner if the groups are examined together.

(1) The Office Action does not list the claims in each group or classify the groups

Pursuant to MPEP § 817, the Office Action should list the claims in each group and classify each group. However, the present Office Action fails to do either. As a result, the restriction is not clear. Although Applicants elected Group iv, it is unknown which claims would be examined in this application. It is also unclear which claims can be pursued in a divisional application should Applicants wish to file any.

(2) The reasons of "unrelated inventions" provided by the Office Action are inconsistent with the claimed invention

The Office Action states that Groups i, ii and v-xiv are unrelated to Group iii because the viruses of Groups i, ii and v-xiv are allegedly not disclosed as capable of being used with the different types of cancer from Group iii. The Office Action further states that the ability to preferentially infect ras-activated neoplasms "provides the listed viruses with a different effect than the cancer types from Group iii" (page 4 of the Office Action). As explained below, these statements are inconsistent with the claimed invention.

Claim 1 is directed to a method of detecting ras-activated neoplastic cells in a biological sample, comprising contacting the sample with a reovirus and determining the ability of the reovirus to replicate in the sample, wherein the ability of the reovirus to replicate indicates the presence of ras-activated neoplastic cells in the sample. Thus, any reovirus, such as the reoviruses recited in claims 4-7, can be used to test any kind of biological sample, such as biological samples obtained from the cancer types of claim 8. A "ras-activated neoplasm" can be any neoplasm in which the ras pathway is activated, which may occur in any place in the body, including the cancer types listed in claim 8. For example, the present application discloses that the ras oncogene accounts for a large number of tumors, including pancreatic tumor, sporadic

colorectal tumor, lung carcinoma, leukemia, breast cancer, gliomas, and glioblastomas (see, e.g., [0023] on page 3). Any other cancer may similarly have an activated ras pathway at the molecular level. Therefore, the viruses of Groups i, ii and v-xiv can be used with the different types of cancer from Group iii.

Similarly, the viruses of Groups i, ii and v-xiv can be used with the different types of cancer from Group xv.

The Office Action further states that Group iii is unrelated to Group xv because the function of the cancer types of Group iii is to "define a population of patients for obtaining a sample", which is unlike the function of the neoplastic phenotypes of Group xv, "which classify a type of cancer as belonging to a certain signaling pathway." Applicants do not fully understand this reasoning. However, as is the case above, the phenotypes of Group xv, which involve the molecular mechanisms of the neoplasms, may appear in any cancer type of Group iii. For example, a breast cancer may have the phenotype of interferon-resistance, p53-deficiency, Rb-deficiency or PKR-deficiency. A lung cancer may also have any of these phenotypes. Therefore, these two groups should not be separated.

(3) There will not be a serious burden on the Examiner if the groups are examined together

There are two criteria for a proper requirement for restriction between patentably distinct inventions:

(a) The inventions must be independent or distinct as claimed; and

(b) There must be a serious burden on the Examiner if restriction is not required.

MPEP §803. If the search and examination of an entire application can be made without serious burden, the Examiner must examine it on the merits, even though it includes claims to independent or distinct inventions. *Id.*

The only ground that the Office Action offers for the restriction of Groups i-xxvii is that the groups are "unrelated" to one another, citing MPEP §§ 806.04 and 808.01. However, even if

the groups are indeed "unrelated" (independent), there would not be a serious burden on the Examiner if the groups are examined together. Notably, Groups i, ii, and iv are drawn to contacting the sample with serotype 3 Dearing strain reovirus, avian reovirus, and reovirus, respectively, and examining them together will not be burdensome. Furthermore, all the viruses of Groups i, ii, iv-xi have a specificity for ras-activated neoplastic cells, thus they can be examined together without a serious burden. All the viruses of Group i, ii and v-xiv are oncolytic viruses, which selectively infect neoplastic cells but not normal cells. Therefore, for the purpose of examining the claimed invention, which relates to selective infection of neoplastic cells rather than the different immunogenicity or surface protein of each virus, all the viruses can be examined together. If there is difficulty in searching all the viruses at the same time, it is suggested that the Examiner issue a species election requirement.

For the foregoing reasons, Applicants request that the restriction of Groups i-xxvii be withdrawn, and optionally replaced with species election requirement(s).

Early examination of this application on the merits is earnestly solicited. In the event that a telephone conversation could expedite the prosecution of this application, the Examiner is requested to call the undersigned at (650) 839-5044.

Please apply any charges or credits to Deposit Account 06-1050.

Respectfully submitted,

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